

## REMARKS

Following entry of this amendment, claims 8 and 29 to 34 are pending in the application. Claim 8 is withdrawn from consideration. Claim 29 has been amended. Claim 34 has been added. Support for the amendment to claim 29 can be found in the specification, e.g., at page 5, lines 9-21; at page 4, lines 21-30; and at original claims 10-12. Support for new claim 34 can be found in the specification, e.g., at page 29, lines 12-14. The amendment to claim 29 and new claim 34 add no new matter.

### Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 29-33 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Action at page 2. Specifically, the Examiner alleged that "[i]t is unclear how the [second] subpopulation differs from the [first subpopulation in claim 29], thus how there can be 'at least two subpopulations.' For example, both parts (a) and (b) are directed to the same outcome, thus there would only be one subpopulation." Action at page 3.

Applicants respectfully traverse. However, solely to expedite prosecution and without acquiescing to the rejection, applicants have amended claim 29 to recite:

29. A library of cultured eucaryotic cells comprising at least two subpopulations of cells, wherein the at least two subpopulations of cells comprises

(a) a first subpopulation of cells, wherein cells of the first subpopulation have a first vector integrated nonspecifically into their genomes, wherein the first vector mediates the splicing of a foreign exon internal to a cellular transcript, and wherein the first vector comprises:

- (i) a foreign exon,
- (ii) a splice acceptor site operatively positioned 5' to said foreign exon, and
- (iii) a splice donor site operatively positioned 3' to said foreign exon,

wherein the first vector does not comprise a promoter operatively positioned 5' to said foreign exon; and

(b) a second subpopulation of cells, wherein cells of the second subpopulation have a second vector integrated nonspecifically into their genomes, wherein the second vector mediates the splicing of a foreign exon 5' to an exon of a cellular transcript, and wherein the second vector comprises:

- (i) a foreign exon,
- (ii) a promoter operatively positioned 5' to said foreign exon,
- (iii) a splice donor site operatively positioned 3' to said foreign exon; and
- (iv) a mutagenic foreign polynucleotide sequence located upstream from said promoter.

Each of claims 30-33 ultimately depends from claim 29. New claim 34 also depends from claim 29.

Applicants have amended claim 29 to even more clearly recite that the first vector and the second vector are not the same. For example, the second vector comprises "a promoter operatively positioned 5' to said foreign exon," while the first vector "does not comprise a promoter operatively positioned 5' to said foreign exon." Applicants assert that amended claim 29 is definite.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

#### Rejections under 35 U.S.C. § 102

##### Nussaume

The Examiner rejected claim 29 under 35 U.S.C. § 102(a) as allegedly "being anticipated by Nussaume et al. (Mol. Gen Genet., Nov. 1995; 249: 91-101; hereinafter Nussaume)." Action at page 3. Specifically, the Examiner alleged that

Nussaume teaches that this "gene trap" method allows cloning of genes (i.e., producing an index of genes or a library). (p. 91, col. 2, last ¶). Furthermore, the gene trap is used to transform eukaryotic cells

(*Arabidopsis*) where splicing can be initiated from the splice donor side (Id.). Therefore the fusion construct produced would necessarily have the foreign exon (i.e. reporter gene) fused to the 3' cellular transcript (i.e. the reporter is 5' to the cellular transcript). In short, Nussaume anticipates claim 29.

Action at pages 3 to 4.

Applicants respectfully traverse. Solely to expedite prosecution and without acquiescing to the rejection, applicants have amended claim 29 as discussed above.

Applicants assert that Nussaume fails to teach a "library of cultured eucaryotic cells comprising at least two subpopulations of cells . . . wherein cells of the first subpopulation have a first vector integrated nonspecifically into their genomes . . . [and] wherein cells of the second subpopulation have a second vector integrated nonspecifically into their genomes" according to claim 29. As discussed above, the first vector and the second vector recited in claim 29 are different. Nussaume only discusses a single gene trap vector, e.g., at Figure 2. For at least that reason, Nussaume fails to teach every element of claim 29, and thus, Nussaume cannot anticipate that claim.

Applicants respectfully request reconsideration and withdrawal of the rejection of claim 29 under 35 U.S.C. § 102(a) over Nussaume.

#### Yoshida

The Examiner rejected claims 29-33 under 35 U.S.C. § 102(b) as allegedly "being anticipated by Yoshida et al. (Transgenic Research, July 1995; 4: 277-87; hereinafter Yoshida)." Action at page 4. Specifically, the Examiner alleged that "Yoshida teaches a 'gene trapping' method in embryonic stem (ES) cells to identify a series of cell clones (i.e. library), wherein the cells have a gene trapping vector

integrated nonspecifically (p. 278, col. 1, even in genes that are not being expressed. (e.g. Abstract, p. 278, col. 1, bottom ¶).” *Id.*

Applicants respectfully traverse. Solely to expedite prosecution and without acquiescing to the rejection, applicants have amended claim 29 as discussed above. Claims 30-33 each ultimately depends from claim 29. New claim 34 also depends from claim 29.

Applicants assert that Yoshida fails to teach a “library of cultured eucaryotic cells comprising at least two subpopulations of cells . . . wherein cells of the first subpopulation have a first vector integrated nonspecifically into their genomes . . . [and] wherein cells of the second subpopulation have a second vector integrated nonspecifically into their genomes” according to claim 29. As discussed above, the first vector and the second vector recited in claim 29 are different. Yoshida only discusses a single gene trap vector, e.g., at Figure 1(A). For at least that reason, Yoshida fails to teach every element of claim 29, and thus, Yoshida cannot anticipate that claim. Moreover, Yoshida cannot anticipate claims 30-34, each of which ultimately depends from claim 29.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) over Yoshida.

#### Double Patenting Rejections

##### U.S. Patent No. 6,136,566

The Examiner rejected claims 29-33 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-7 and

10 of U.S. Patent No. 6,136,566 (the '566 patent). Action at page 5. Solely to expedite prosecution and without acquiescing to the rejection, applicants submit a Terminal Disclaimer concerning the '566 patent and the required fee of \$110.00.

Applicants respectfully request reconsideration and withdrawal of the double patenting rejection in view of the '566 patent.

U.S. Patent No. 6,207,371

The Examiner rejected claims 29-33 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-7, 25-28, and 37 of U.S. Patent No. 6,207,371 (the '371 patent). Action at page 6. Solely to expedite prosecution and without acquiescing to the rejection, applicants submit a Terminal Disclaimer concerning the '371 patent and the required fee of \$110.00.

Applicants respectfully request reconsideration and withdrawal of the double patenting rejection in view of the '371 patent.

Applicants respectfully request reconsideration and withdrawal of all outstanding rejections. Applicants respectfully assert that the present application is in condition for allowance and request that the Examiner issue a timely Notice of Allowance. If the Examiner does not consider the application to be allowable, the undersigned requests that, prior to taking action, the Examiner call her at (650) 849-6656 to set up an interview.

Please grant any extensions of time required to enter this Amendment and  
Response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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GARRETT & DUNNER, L.L.P.

Dated: June 10, 2004

By: 

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